REMARKS

Claims 1-19, 21, 31, 32, 41-43, 52, 53 and 57-61 are pending in the subject application.

Double Patenting

On page 2 of the September 22, 2006 Final Office Action, the Examiner provisionally rejected claims 1-19, 21, 31, 32, 41-43, 52, 53 and 57-61 under the doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-14, 16, 24, 25, 27, 36, 37, 47 and 52 of copending Application No. 10/758,397 (U.S. Patent Application Publication 2005/0008634 A1).

In response, applicants respectfully request withdrawal of the provisional obviousness-type double patenting rejection in this application because a provisional obviousness-type double patenting rejection cannot be maintained in an application if it is the sole rejection. See, e.g. M.P.E.P. §804(I)(B), last paragraph. Applicants look forward to the withdrawal of the only other rejection under 35 U.S.C. § 103, as discussed below.

Thus, this application should be in condition for allowance, whereas a first Office Action has only recently issued in copending U.S. Serial No. 10/758,397 to which applicants have not yet responded.

For the forgoing reasons, the provisional obviousness-type double patenting rejection should be withdrawn in the subject application.

Rejections Under 35 U.S.C. §103

On pages 3-4, in Sections 5-8 of the September 22, 2006 Final Office Action, the Examiner has maintained the rejections of the claims under 35 U.S.C. § 103. Specifically, the Examiner maintained the rejection of:

-claims 1-4, 7, 8, 11, 19, 21 and 31 under 35 U.S.C. §103(a) as unpatentable over U.S. Patent Application Publication No. 2004/0127408 A1 to Mozes ("Mozes") in view of U.S. Patent No. 5,997,856 to Hora et al. ("the '856 patent");

-claims 5 and 6 under 35 U.S.C. § 103 over Mozes in view of the '856 patent as applied to claims 1-4, 7, 8, 11, 31, 42, 53, 57 and 59-61 and in further view of Anderson, B.D. and Flora, K.P. (Chapter 34, pages 739-754, *The Practice of Medicinal Chemistry*, edited by Camilles Georges Wermuth, Academic Press 1996); and

-claims 9, 10 and 12-18 under 35 U.S.C. § 103 over Mozes in view of the '856 patent as applied to claims 1-4, 7, 8, 11 and 31 and further in view of U.S. Patent No. 5,134,127 to Stella et al. ("the '127 patent").

Applicants' Reply

In response, Applicants respectfully maintain that the combination of references is improper, and even if it were proper fails to satisfy the requirements of an obviousness rejection.

Applicants respectfully submit that the obviousness rejections maintained in the September 22, 2006 Final Office Action fail to satisfy at least the following elements of the legal standard of an obviousness rejection:

1. THE PRIOR ART FAILS TO IDENTIFY A SOLUBILITY PROBLEM WITH THE POLYPEPTIDE RECITED IN THE PENDING CLAIMS.

The September 22, 2006 Final Office Action, to purportedly show existence of motivation, referred to paragraph [0088] of the Mozes application, presumably to the last sentence of the paragraph. This sentence, however, a) does not indicate that there is any solubility problem, and b) teaches that "derivatives and salts" can "modify . . . stability, solubility, etc." A cyclodextrin as claimed by Applicants is neither "derivatives" nor "salts". Applicants, therefore, maintain that the need for a cyclodextrin, or of any solubility enhancer at all, is simply not taught or alluded to by the Mozes application.

Absent knowledge of a solubility problem, one skilled in the art had no motivation to look for any solution. Thus, absent Applicants' disclosure, there is nothing of record except hindsight motivating the combination of the peptide of Mozes with any solubility enhancer, much less the ones of the '856 patent. This is a fundamental deficiency of the obviousness rejection of record.

2. THE PRIOR ART FAILS TO TEACH SELECTION OF CYCLODEXTRINS FROM AMONG THE MULTITUDE OF SOLUBILITY ENHANCERS.

Cyclodextrins are not a common class of solubility enhancers. Cyclodextrins have known problems, as explained on pages 14-15 of Applicants' July 27, 2006 Amendment. The September 22, 2006 Final Office Action did not dispute this.

The primary reference, Mozes, does not indicate there is a need for any solubility enhancer, and certainly does not suggest a need for cyclodextrins. If anything, Mozes teaches in its

paragraph [0088] that solubility and stability can be modified by making "derivatives and salts" of the peptide. A cyclodextrin as claimed by Applicants is neither "derivatives" nor "salts".

Therefore, the art fails to teach or suggest to one skilled in the art the selection of cyclodextrins for use with the recited peptide.

3. THE PRIOR ART FAILS TO PROVIDE AN EXPECTATION THAT THE COMBINATION OF CYCLODEXTRIN WITH THE SPECIFIC RECITED PEPTIDE WOULD IMPROVE SOLUBILITY OF THE RECITED PEPTIDE.

Whether any given solubility enhancer would be effective for a given peptide class cannot be predicted. The September 22, 2006 Final Office Action did not dispute this.

For example, applicants needed to test over 40 solubility enhancers to find several that could improve the solubility of the recited peptide. See, pages 23-31 of the subject application. Table 2, part B of Hora shows that cyclodextrins are not universally effective (only 2 of the 4 protein formulations passed a visual solubility test).

Therefore, one of skill would not expect that the solubility of the recited peptide would be improved by cyclodextrins.

4. THE PRIOR ART FAILS TO PROVIDE AN EXPECTATION THAT THE COMBINATION OF CYCLODEXTRIN WITH THE SPECIFIC RECITED PEPTIDE WOULD RESULT IN A BIOLOGICALLY ACTIVE PHARMACEUTICAL COMPOSITION.

Even if a solubility enhancer improves the solubility of a peptide, one of skill would not expect the resulting composition

to necessarily be biologically active. The September 22, 2006 Final Office Action did not dispute this.

See, for example, Applicants' results with PEG 400, which improved solubility but eliminated biological activity of the recited peptide (page 25, lines 8-12 of the subject application). See, also, Table 3 of Hora showing that 2 of the three formulations with cyclodextrin had significantly reduced bioactivity (36% and 45% less!), and a fourth one with insulin that *was not even shown*.

Clearly, therefore, the prior art did not provide the expectation of success necessary for a proper obviousness rejection.

Applicants note the September 22, 2006 Final Office Action relies on Stella et al. to assert that cyclodextrins "reduced toxicity, and reduced membrane disruption …." However, Stella et al. do not teach that a cyclodextrin always maintains bioactivity of the compound. More importantly, Stella et al. deal with small molecule drugs, and clearly cannot offer any teaching relevant to peptides, much less relevant to the claimed peptide.

Conclusion

In conclusion, Applicants respectfully maintain that the claimed invention is inventive over the prior art. Applicants also maintain that the obviousness rejections of record are fundamentally deficient for any one of the four reasons discussed above. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections.

If the Examiner has any questions about the patentability of the pending claims after consideration of remarks herein, Applicants respectfully request an interview with the Examiner to

efficiently advance prosecution. Applicants' undersigned attorneys invite the Examiner to telephone at the number provided below.

No fee is deemed necessary in connection with the filing of this Response. However, if any other fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,

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